UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/503,559	02/11/2000	Roland Valdes JR.	1160.033US1	6803

21186 7590 10/01/2002

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/01/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/503,559	VALDES ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *10-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *10* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Ulrike Winkler, Group Art Unit 1648.

Election/Restrictions

Applicant's election without traverse of Group I in Paper No. 9 is acknowledged. Upon review and reconsideration of the prior Election/Restriction requirement the following new restriction requirement is made. The Office apologizes for any inconvenience this may have caused applicant. In order to facilitate prosecution the Office made a telephone call to Ann Viksnins on September 23, 2002 to provide applicant with an opportunity of making a provisional election based on the new groups.

The new Election/ Restriction requirement is as follows:

I. Claims 1-9, drawn to a purified dihydroouabain-like factor, classified in class 536, subclass 6.1.

II. Claims 10-20, drawn to a method of treating a condition with the dihydroouabain-like factor, classified in class 424, subclass 1.73.

III. Claims 21-23, drawn to an antibody directed to the factor derived from a mammalian source, classified in class 530, subclass 389.1.

IV. Claims 24-26, drawn to a method of treatment using the antibody, classified in class 424, subclass 134.1.

V. Claims 27-28, drawn to a method of detecting dihydroouabain-like factor, classified in class 435, subclass 7.1.

VI. Claims 30-31, drawn to a method of purifying dihydroouabain-like factor using HPLC, classified in class 536, subclass 127.

VII. Claims 32-33, drawn to a plant derived dihydroouabain isomer, classified in class 536, subclass 6.3.

The inventions are distinct, each from the other because of the following reasons:

Groups I, II and VII are compositions and are distinct from groups II, IV, V and VI which are drawn to methods. Groups I, II and VII are compositions and each is distinct from the other because they contain different materials. Group I comprises a dihydroouabain-like factor. Group II comprises an antibody, which is made up of amino acids. Group III is a plant dihydroouabain isomer. Though there may be overlap for these groups, the search for one group will not be coextensive with that of the other group.

Groups II, IV, V and VI are drawn to methods and each is distinct from the other because they utilize different starting materials, therefore the outcomes are not be expected to be the same. Group II is drawn to a method of treatment using a dihydroouabain-like factor. Group III is drawn to a method of treatment using an antibody. Group IV is drawn to a method of detecting a dihydroouabain-like factor while group VI is a method of purifying a dihydroouabain-like factor. Though there may be overlap between the methods in question for groups II, IV, V and VI, each utilizes different starting materials and techniques, therefore the outcome is expected to be different.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the treatment for hypertension can be achieved with a materially different product such as Valsartan, quinapril hydrochloride or Nadolol to name a few.

Inventions III and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the treatment for hypertension can be achieved with a materially different product such as Valsartan, quinapril hydrochloride or Nadolol to name a few.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that a rejoinder of claims is possible at a later date if the product is eventually found patentable. Guidance on treatment of product and process claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b) is set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86.

> To facilitate examination under § 103, where product and process claims are presented in the same application, applicant may be called upon under 35 U.S.C. § 121 to elect claims to either the product or process. The claims to the non-elected invention will be withdrawn from further consideration. However, in the case of an elected product claim,

> rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

During a telephone conversation with Ann Viksnins on September 23, 2002 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-9. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10-34 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 5, is attached to the instant Office Action.

Claim Objections

Claims 2 and 4 are objected to because of the following informalities: The instant claim makes reference to dho, however, the abbreviation dho has not been identified in the claim. The specification on page 7, line 4 identifies dho as being plant derived dihydroouabain. Applicant is requested to identify dho in the claims so that the claims may be understood without the need to refer to the specification. Applicant's cooperation is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "dihydroouabain-like factor" is indefinite, because the ordinary artisan would not know the metes and bounds of this term. When is a product "dihydroouabain-like" and when does it fall outside the scope of being "dihydroouabain-like". Looking to the specification it is not clear that there are distinct structural differences between the "dihydroouabain-like factor" and dihydroouabain produced or isolated from any other source, such as plant. The specification and the claims (claims 2 and 3) use modifiers such as "similar to" and "substantial", these modifiers do not provide direction to allow the ordinary artisan to determine the metes and bounds of the term "dihydroouabain-like factor" as they do not provide set limitations. The specification on page 29 indicates that the HPLC pattern for the "dihydroouabain-like factor" and the "ouabain-like factor" is "similar to" the pattern observed for the plant derived dihydroouabain or ouabain, the same is true for the UV spectral analysis of the compounds. "Similar" is defined in the dictionary as having characteristics in common, strictly comparable, alike in substance or essentials or having the same shape but differing in size or proportions. Therefore, compounds that are the same would fall within the scope being "similar to". The art defines dihydroouabain as the product of reduction of ouabain wherein the lactone ring is fully hydrogenated. Hamylyn et al. (Identification and characterization of a ouabain –like compound from human plasma, Proceedings of the National Academy of Sciences,

(1991) Vol. 88 pp. 6259-6263, see discussion 1st paragraph) have purified a "ouabain-like factor" from human plasma and bovine adrenal glands and found that the mammalian derived "ouabain-like compound" is indistinguishable structurally, biologically and immunologically from the plant derived ouabain. The instantly claimed "dihydroouabain-like factor" is derived from the same tissues as the prior art "ouabain-like factor". Given the similarities based on UV spectra and HPLC elution data between the plant derived dihydroouabain and the mammalian derived "dihydroouabain-like factor" as disclosed in the specification it is not clear what the structural differences are between the claimed "dihydroouabain-like factor" and dihydroouabain from a plant source. Therefore, the term "dihydroouabain-like factor" is indefinite because the term implies a difference that cannot be determined. For purposes of the instant office action dihydroouabain is interpreted to fall within the scope of the definition of the "dihydroouabain-like factor".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Klaus Repenning (U.S. Pat. No. 3,113,128).

The instant invention is drawn to a purified "dihydroouabain-like factor" which encompasses dihydroouabain (see above). For this office action, the product-by-process claims

were interpreted as "a composition of matter" (which are *products*, wherein the chemical nature of the substances or materials used is the distinguishing characteristic). Product-by-process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113 states that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

K. Repenning disclose the production of chemically pure dihydroouabain by chemically reducing strophanthin also know as ouabain a resin like glycoside. Strophanthin (according to Webster's dictionary) is a term that refers to glycosides (such as ouabain) which are derived from the seed or leaves of African plants belonging the genus *Strophanthus* or *Acokanther*. The patent discloses the use of dihydroouabain as a pharmaceutical (see column 1, line 17-24) which it would have to be formulated in such a way so that it may be administered to a patient. The patent discloses the reduction of strophanthin/ouabain to obtain dihydroouabain and the steps involved in the purification of dihydroouabain via extractions. The reference also discloses that the reactivity of dihydroouabain is not as strong as that of ouabain. This reduced reactivity is beneficial because it will prevent accidental overdosing of a patient. The reference discloses that prior dihydroouabain compositions (see Jacobs et al. Journal of Biological Chemistry, 1927, cited in the patent) were not suitable for therapeutic purposes because the compound was unstable and caused fluctuations in the effectiveness due to their low stability. In the incorporated reference (Jacobs et al.) dihydroouabain was found to be 16.1 fold less effective

than ouabain as based on their toxicity in frogs and the reference indicates that there are fluctuations in the toxicity of dihydroouabain depending on the preparation used. Therefore, the limitation of a 10 fold lower potency than a ouabain-like factor and a 3 fold higher potency as compared to plant derived dihydroouabain falls within the fluctuations of dihydroouabain activity observed due to the lack of stability of the compound itself. A recitation of the tissues (human or bovine) from which the factor is isolated as well as the elution pattern from a chromatographic column are process steps. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure dihydroouabain, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The reactivates of the compound to specific antibodies or to the inhibition pattern of the sodium potassium pump are properties of the chemical composition, which depend on their structure. Chemical compounds and their properties are inseparable, therefore, the limitation does not distinguish instant invention over the prior art. See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Therefore, the instant invention is anticipated by K. Repenning.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D. 10/1/02